

EXHIBIT A

# **CURRICULUM VITAE**

**ROBERT M. HOFFMAN**

July 2002

*CURRICULUM VITAE*

**ROBERT M. HOFFMAN**

**OFFICES:** AntiCancer, Inc.  
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Department of Surgery  
University of California, San Diego  
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200 West Arbor Drive  
San Diego, California 92103-8402  
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**BIRTH DATE:** June 19, 1944  
Greenwich, Connecticut

**EDUCATION:** Ph.D. (Biology) 1971  
Harvard University  
Cambridge, Massachusetts

B.A. (Biology) 1965  
State University of New York  
Buffalo, New York

**PRESENT POSITIONS:** President, Chairman of Board and CEO 1984-present  
AntiCancer, Inc.  
San Diego, California

Professor 1995-present  
Department of Surgery  
University of California, San Diego  
Medical Center  
200 West Arbor Drive  
San Diego, California 92103-8220

## MAJOR RESEARCH ACCOMPLISHMENTS:

1. Development of highly-selective anti-methionine cancer therapy based on methioninase.
2. Development of DNA-containing liposomes (1978) – the enabling technology for non-viral *in vivo* gene therapy.
3. Development of a "patient-like" animal model for cancer – "MetaMouse<sup>®</sup>".
4. Development of an *in vivo*-like model of human tumor culture and drug-sensitivity testing.
5. Development of an *in vitro* hair growth model from human and animal skin.
6. Development of a hair follicle-specific drug and gene targeting system.
7. Discovery of the governing step of metastasis.
8. Development of whole-body fluorescence imaging for cancer metastasis, gene expression, and bacterial infection.
9. Development of enzyme-activated prodrug gene therapy with the methioninase gene and selenomethionine.
10. Development of the concept of cancer epigenetics (1984).
11. Development of the first single enzyme assay for homocysteine.
12. Development of the first homogeneous assay for vitamin B<sub>6</sub>.

## POSTDOCTORAL TRAINING:

Department of Biology Harvard University With the late Professor John R. Raper	1971-1973
Massachusetts General Hospital	1973-1975
Harvard Medical School With Dr. Richard W. Erbe and Professor John W. Littlefield	1976-1977
The Shemyakin Institute of Bioorganic Chemistry Academy of Sciences, Moscow, USSR With Professor L.D. Bergelson	1976-1977
Weizmann Institute of Science Rehovot, Israel With Dr. Carol Prives	1978

## PREVIOUS ACADEMIC POSITIONS:

Instructor of Pediatrics Harvard Medical School Massachusetts General Hospital	1975-1979
Assistant Professor, Department of Pediatrics University of California, San Diego, School of Medicine School of Medicine	1979-1983

Associate Professor, Department of Pediatrics University of California, San Diego School of Medicine	1983-1990
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Professor, Department of Pediatrics University of California, San Diego School of Medicine	1990-1995
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## PROFESSIONAL SOCIETIES:

1. Society for *In Vitro* Biology
2. American Association of Cancer Research
3. American Society for Clinical Oncology
4. Society of Surgical Oncology
5. American Society for Cell Biology
6. Metastasis Research Society
7. Japanese Cancer Association
8. Japanese Metastasis Research Society
9. Japanese Society of Human Cell
10. Preclinical Therapeutic Model Group of the European Organization for Research and Treatment of Cancer

## BOARDS:

Ad-Hoc Reviewer National Cancer Institute	1986-present
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## EDITORIAL BOARDS:

<i>Anticancer Research</i>	1985-present
<i>In Vitro Cellular and Developmental Biology</i>	1987-present
Associate Editor, <i>Clinical Cancer Research</i>	2000-Present

## TEACHING AT THE UNIVERSITY OF CALIFORNIA, SAN DIEGO:

Biology 112:	"Cell and Molecular Biology" Spring and Fall With Professor Gordon Sato	1980
Pediatrics 233:	"Genes and Cancer" Winter	1982-1994
Pediatrics 235:	"New Biological Approaches to Cancer Prevention and Treatment" Spring	1983-1994

Pediatrics 237:	"Biochemical Genetics of Aging"	
	Fall	1984-1994

#### UNIVERSITY COMMITTEES:

Admissions Committee	1983-1985
University of California, San Diego	
School of Medicine	

Electives Committee	1989-1990
University of California, San Diego	
School of Medicine	

#### HONORS AND AWARDS:

Honorary Professor	1994
Harbin Medical University	
Harbin, China	

Honorary Member	1991
Keio University Department of Surgery	
Tokyo, Japan	

A.N. Belozersky Medal	1990
Moscow State University	

Research Career Development Award	1982-1987
National Cancer Institute	

Fellow of the Leukemia Society of America	1979-1981
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Fellow of the Medical Foundation of Boston	1976-1977
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United States National Academy of Sciences	1976-1977
Exchange Fellowship	
Shemyakin Institute of Bioorganic Chemistry	
Moscow, USSR.	

Postdoctoral Fellowship Awardee	1974,76,78
National Institutes of Health	

National Institutes of Health	1973-1974
Postdoctoral Training Grant Fellow	
Harvard Medical School	

Postdoctoral Research Fellow	1971-1973
Harvard University	

National Institutes of Health Training Grant Predoctoral Fellowship Harvard University	1966-1971
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Phi Beta Kappa State University of New York Buffalo, New York	1964
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**PLENARY LECTURES:**

International Symposium on "The biochemistry of S-adenosylmethionine as a basis of drug design" Bergen Norway Lecture entitled "Cancer, methionine and transmethylation. "	1985
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Federation of American Societies for Experimental Biology Summer Research Conference entitled "Folic acid, B-12, and one-carbon metabolism" Saxtons River, Vermont Lecture entitled "Altered methionine metabolism and transmethylation in human cancer cells."	1986
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Gordon Research Conference on Cancer New London, New Hampshire Lecture entitled "Methionine, transmethylation and cancer."	1987
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Invited lecturer, Tissue Culture Association Conference Las Vegas, Nevada Lecture entitled "Partitioning of methyl groups in cancer and normal cell types. "	1988
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Federation of American Societies for Experimental Biology Summer Research Conference Copper Mountain, Colorado Lecture entitled "Cancer, methionine metabolism and transmethylation."	1989
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Invited Lecturer, Dae Han Biochemical Society Seoul, Korea Lecture entitled "Altered methionine metabolism, unbalanced global cellular transmethylation and cancer."	1990
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Invited Lecturer, Korean Association of Molecular Biology Pusan, Korea Lecture entitled "Rational evaluation and design of cancer drugs. "	1990
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<p>Third International Conference of Anticancer Research  Marathon, Greece  Lecture entitled "The development of clinically relevant in vitro and m vivo preclinical models: Three-dimensional gel-supported in vitro histoculture and orthotopic implantation and metastasis of human tumors in nude mice. "</p>	1990
<p>Invited Lecturer, Regina Elena Cancer Center  Rome, Italy  Lecture entitled "Patient-like in vitro and in vivo pre-clinical models of human cancer."</p>	1991
<p>Gordon Research Conference on Cancer Chemotherapy  New London, New Hampshire  Lecture entitled "Orthotopic-transplantation animal models for the identification of new anticancer drugs. "</p>	1992
<p>Fourth International Congress of the Metastasis Research Society  Paris, France  Lecture entitled "The nude mouse comes to the cancer clinic: Metastatic models of the major cancer types constructed by orthotopic transplantation of histologically-intact patient specimens."</p>	1992
<p>First Congress of the International Society for Experimental Microsurgery  Rome, Italy  Lecture entitled "Microsurgery, orthotopic human tumor transplantation and the nude mouse: Patent-like metastatic models of human cancer. "</p>	1992
<p>Keystone Symposium on Discovery and Development of Therapeutic Compounds  Snowmass, Colorado  Session Chairman., Lecture entitled "Orthotopic models for treatment evaluation in vivo using histologically-intact cancer patient specimens."</p>	1993
<p>FASEB Summer Conference  Copper Mountain, Colorado  Lecture entitled "MetaMouse<sup>®</sup>: the nude mouse comes to the cancer clinic via orthotopic transplantation of architecturally-intact patient tumors. "</p>	1993
<p>Hellenic Society For Breast Cancer Research, First Int'l Congress  Corfu, Greece  Lecture entitled "Patient-like cancer models and therapeutics specific for cancer- an approach to the next generation of treatment"</p>	1993
<p>FASEB Summer Conference  Copper Mountain, Colorado  Lecture entitled "Tissue architecture and metastases"</p>	1994



Japan Society of Human Cell Meeting Toyoma City, Japan Lecture entitled "In vitro drug response assays are clinically useful in cancer"	1995
Hellenic Society For Breast Cancer Research, Second Int'l Congress Kos Island, Greece Lecture entitled "Methioninase (AC9301): A selective antitumor agent with a new mechanism of action."	1995
6th International Congress on Anticancer Treatments Paris, France Lecture entitled "Pilot phase I clinical trial of methioninase: serum depletion of methionine without acute toxicity."	1996
6th International Congress on Anticancer Treatments Paris, France Lecture entitled "The gelatinase-A Inhibitor CT1746 arrests human colon tumor growth and spread and increases survival in a patient like orthotopic model in nude mice."	1996
IBC USA Alopecia Conference San Diego, California Lecture entitled "The feasibility of targeted selective gene therapy of the hair follicle."	1996
Shanghai International Symposium on Liver Cancer & Hepatitis Shanghai, China Lecture entitled "Liver colonization capability governs metastatic potential"	1996
Cambridge Healthtech Institute's Engineered Animal Models Baltimore, Maryland Lecture entitled "MetaMouse <sup>®</sup> Models of Cancer: Clinically Relevant Orthotopic Models of Cancer Growth and Metastasis"	1996
Third International Conference of the Asian Clinical Oncology Society (ACOS) Kunming, China Lecture entitled "Taking chemotherapy from random to rational with the histoculture drug response assay"	1996
The International Congress on Human Cell and Cell Culture Tokyo, Japan Lecture entitled "Nutritional regulation of cancer growth by use of methioninase: possible apoptotic cell kill mechanism"	1996

<p>The Sixth International Congress of the Metastasis Research Society Gent, Belgium</p> <p>Lecture entitled “Surgical Orthotopic Implantation (SOI): A new approach to develop clinically-relevant models of human metastatic cancer in immunodeficient rodents”</p>	1996
<p>IBC’s Alopecia Conference Washington, D.C.</p> <p>Lecture entitled “Hair Follicle Targeting of Large and Small Molecules with Topical Liposomes”</p>	1996
<p>First Panhellenic Congress of Tumors Markers with International Participation Athens, Greece</p> <p>Lecture entitled “Methionine dependence as a Possible Universal Therapeutic Tumor Marker”</p>	1996
<p>Seventh International Congress on Anticancer Treatment (SOMPS) Paris, France</p> <p>Lecture entitled “R-Methioninase as a potential universal apoptotic antitumor agent”</p>	1997
<p>Seventh International Congress on Anticancer Treatment (SOMPS) Paris, France</p> <p>Lecture entitled “Acquisition of broad range multidrug resistance in recurrent breast cancer”</p>	1997
<p>IBC’s Drug Discovery Approaches to Cosmeceuticals Conference East Rutherford, NJ</p> <p>Lecture entitled “Hair producing histoculture skin for the discovery of a new generation of hair follicle targeted cosmeceuticals and therapeutics</p>	1997
<p>30th Annual Meeting of the Japanese Research Society for Appropriate Cancer Chemotherapy Tokyo, Japan</p> <p>Lecture entitled “Histoculture Drug Response Assay”</p>	1997
<p>IBC’s Delivery Technologies for Cosmetic Ingredients Conference Philadelphia, PA</p> <p>Lecture entitled “Cosmetic and therapeutic molecules targeted to hair follicles by topical liposomal application”</p>	1997
<p>6th Hellenic Congress on Senology and the 3rd International Congress of the Hellenic Society for Breast Cancer Research Alexandroupolis, Greece</p> <p>Lecture entitled “Cachexia in breast cancer and elevated amino-acid requirements of tumors: Selective biological targets for therapy”</p>	1997

FASEB Summer Research Conference on Biological Methylation Saxtons River, Vermont Lecture entitled "Alterations in methionine dependence and transmethylation in cancer: methioninase for therapy"	1997
3 <sup>rd</sup> International Symposium on Polymer Therapeutics London, England Lecture entitled "Polyethylene glycol conjugation of recombinant methioninase for cancer therapy"	1998
8 <sup>th</sup> International Congress on Anti-Cancer Treatment Paris, France Lecture entitled "Polyethylene glycol conjugation of recombinant methioninase for cancer therapy"	1998
Gordon Research Conference on Lasers in Medicine and Biology Meriden, NH Lecture entitled "Green fluorescent protein: A new light to study metastasis and angiogenesis"	1998
25 <sup>th</sup> Balken Medical Week Conference Ioannina, Greece Lecture entitled "Methioninase: A new selective cancer therapy"	1998
7 <sup>th</sup> Annual Meeting of the Japanese Association for Metastasis Research Sapporo, Japan Lecture entitled "Green fluorescent protein: A new light to study the role of angiogenesis in metastasis"	1998
SPIE's International Symposium on Biomedical Optics San Jose, CA Lecture entitled "Green fluorescent protein: A new light to visualize metastasis and angiogenesis in cancer"	1999
2 <sup>nd</sup> International Symposium on GFP – The Green Fluorescent Protein San Diego, CA Lecture entitled "Fluorescent optical tumor imaging (FOTI) of human cancers in live nude mice"	1999
4 <sup>th</sup> International Conference of the Asian Clinical Oncology Society (ACOS) Bali, Indonesia Lecture entitled "Individualizing cancer chemotherapy by tumor histoculture"	1999

58 <sup>th</sup> Annual Meeting of the Japanese Cancer Association Hiroshima, Japan Lecture entitled “Orthotopic transplant mouse models with green fluorescent protein-expressing cancer cells to visualize micrometastasis and angiogenesis”	1999
SPIE’s International Symposium on Biomedical Optics San Jose, CA Lecture entitled “External optical imaging of green fluorescent protein-expressing metastatic tumors”	2000
VIII International Congress of the Metastasis Research Society London, UK Lecture entitled “GFP tumor, metastases, and angiogenesis whole-body imaging”	2000
9 <sup>th</sup> Shizuoka Drug Delivery Conference Shizuoka, Japan Lecture entitled “Polyethylene glycol conjugation of recombinant methioninase for cancer therapy”	2000
World Congress on In Vitro Biology San Diego, California Lecture entitled “Individualized cancer chemotherapy by tumor histoculture”	2000
13 <sup>th</sup> International Congress on Photobiology San Francisco, California Lecture entitled “In vivo high-throughput drug screen with whole-body imaging GFP tumor models”	2000
11 <sup>th</sup> International Symposium for Bioluminescence and Chemiluminescence Monterey, California Lecture entitled “Whole-body optical imaging of green fluorescent protein-expressing tumors”	2000
92 <sup>nd</sup> Annual American Association for Cancer Research Annual Meeting Educational Session 7 – Approaches in Drug Development and Toxicology New Orleans, Louisiana Lecture entitled “Whole-body fluorescence imaging of GFP of tumor growth, Metastasis, angiogenesis and gene expression”	2001

### **Publications of Robert M. Hoffman, Ph.D.**

1. Hoffman, R.M., and Raper, J.R. Genetic restriction of energy conservation in *Schizophyllum*. *Science* **171**, 418-419, 1971.
2. Hoffman, R.M. and Raper, J.R. Lowered respiratory response to adenosine diphosphate of mitochondria isolated from a mutant-B strain of *Schizophyllum commune*. *J. Bacteriol.* **110**, 789-791, 1972.
3. Raper, J.R. and Hoffman, R.M. *Schizophyllum commune*. *In: Handbook of Genetics*. **3**, R King (ed.), New York, Plenum Press, 597-626, 1974.
4. Hoffman, R.M. and Raper, J.R. Genetic impairment of energy conservation in development of *schizophyllum*: Efficient mitochondria in energy-starved cells. *J. Gen. Microbiol.* **82**, 67-75, 1974.
5. Hoffman, R.M. and Erbe, R.W. High *in vivo* rates of methionine biosynthesis in transformed human and malignant rat cells auxotrophic for methionine. *Proc. Natl. Acad. Sci. USA* **73**, 1523-1527, 1976.
6. Williams, J., Hoffman, R.M. and Penman, S. The extensive homology between mRNA sequences of normal and SV40-transformed human fibroblasts. *Cell* **11**, 901-907, 1977.
7. Hoffman, R.M., Jacobsen, S. J. and Erbe, R.W. Reversion to methionine independence by malignant rat and SV40-transformed human fibroblasts. *Biochem. Biophys. Res. Commun.* **82**, 228-234, 1978.
8. Hoffman, R.M., Margolis, L.B. and Bergelson, L.D. Binding and entrapment of high molecular weight DNA by lecithin liposomes. *FEBS Letters* **93**, 365-368, 1978.
9. Hoffman, R.M., Jacobsen, S.J. and Erbe, R.W. Reversion to methionine independence in SV40-transformed human and malignant rat fibroblasts is associated with altered ploidy and altered properties of transformation. *Proc. Natl. Acad. Sci., USA* **76**, 1313-1317, 1979.
10. Jacobsen, S.J., Hoffman, R.M. and Erbe, R.W. Regulation of methionine adenosyltransferase in normal diploid and SV40-transformed human fibroblasts. *J. Natl. Cancer Inst.* **65**, 1237-1244, 1980.
11. Hoffman, R.M. and Jacobsen, S.J. Reversible growth arrest in SV40-transformed human fibroblasts. *Proc. Natl. Acad. Sci., USA* **77**, 7306-7310, 1980.
12. Rubnitz, J.E., Jacobsen, S.J. and Hoffman R.M. Constitutive behavior of methionyl-tRNA synthetase compared to repressible behavior of methionine adenosyltransferase in mammalian cells. *Biochem. Biophys. Acta Reviews on Cancer* **577**, 269-273, 1981.

13. Diala, E.S., Plent, M.M., Coalson, D.W. and Hoffman, R.M. DNA methylation in normal and SV40-transformed human fibroblasts. *Biochem Biophys. Res. Commun.* **102**,1379-1384, 1981.
14. Hoffman, R.M., Coalson, D. W., Jacobsen, S.J. and Erbe, R.W. Folate polyglutamate and monoglutamate accumulation in normal and SV40-transformed human fibroblasts. *J. Cell. Physiol.* **109**, 497-505, 1981.
15. Hoffman, R.M. Methionine dependence in cancer cells - a review. *In Vitro* **18**, 421-428, 1982.
16. Coalson, D.W., Mecham, J.O., Stern, P.H., and Hoffman, R.M. Reduced availability of endogenously synthesized methionine for S-adenosylmethionine formation in methionine-dependent cancer cells. *Proc. Nat. Acad. Sci., USA* **79**,4248-4251, 1982.
17. Diala, E.S. and Hoffman, R.M. DNA methylation levels in normal and chemically-transformed mouse 3T3 cells. *Biochem. Biophys. Res. Commun.* **104**, 1489-1494, 1982.
18. Diala, E.S. and Hoffmam, R.M. Hypomethylation of HeLa cell DNA and the absence of 5-methylcytosine in SV40 and adenovirus (type 2) DNA: analysis by HPLC. *Biochem. Biophys. Res. Commun.* **107**, 19-26, 1982.
19. Stern, P.H., Mecham, J. O. and Hoffman, R.M. Preparation of [<sup>35</sup>S]homocysteine thiolactone free of [<sup>35</sup>S]methionme. *J. Biochemical and Biophysical Methods* **7**, 83-88, 1982.
20. Diala, E.S. and Hoffman, R.M. Epstein-Barr HR-1 virion DNA is very highly methylated. *J. Virology* **45**, 482-483, 1983.
21. Stern, P.H., Mecham, J.O., Wallace, C.D. and Hoffman, R.M. Reduced free-methionine in methionine-dependent SV40-transformed human fibroblasts synthesizing apparently normal amounts of methionine. *J. Cell. Physiol.* **117**, 9-14, 1983.
22. Diala, E.S., Cheah, M.S.C., Rowitch, D. and Hoffman, R.M. The extent of DNA methylation in human tumor cells. *J. Natl. Cancer Inst.* **71**, 755-764, 1983.
23. Oden, K.L., Carson, K., Mecham, J.O., Hoffman, R.M. and Clarke, S. S-adenosylmethionine synthetase in cultured normal and oncogenically-transformed human and rat cells. *Biochem. Biophys. Acta* **870**, 270-277, 1983.
24. Mecham, J.O., Rowitch, D., Wallace, C.D., Stern, P.H. and Hoffman, R.M. The metabolic defect of methionine dependence occurs frequently in human tumor cell lines. *Biochem. Biophys. Res. Commun.* **117**, 429-434, 1983.
25. Stern, P.H., Wallace, C.D. and Hoffman, R.M. Altered methionine metabolism occurs in all members of a set of diverse human tumor cell lines. *J. Cell. Physiol.* **119**, 29-34, 1984.
26. Hoffman, R.M. Altered methionine metabolism, DNA methylation and oncogene expression

- in carcinogenesis: a review and synthesis. *Biochem. et Biophys. Acta Reviews on Cancer* **738**, 49-87, 1984.
27. Cheah, M.S.C., Wallace, C.D. and Hoffman, R.M. Hypomethylation of DNA in human cancer cells: a site-specific change in the c-myc oncogene. *J. Natl. Cancer Inst.* **73**, 1057-1065, 1984.
  28. Stern P.H. and Hoffman, R.M. Elevated overall rates of transmethylation in cell lines from diverse human tumors. *In Vitro - Rapid Commun. in Cell Biology* **20**, 663-670, 1984.
  29. Hoffman, R.M. Altered methionine metabolism and transmethylation in cancer. *Anticancer Res.* **5**, 1-30, 1985.
  30. Hoffman, R.M. and Stern, P.H. Cancer, methionine and transmethylation. In *Biological Methylation and Drug Design*, Borchardt, R.T., Creveling C.R. and Ueland, P.M, eds., Clifton, New Jersey, The Humana Press Inc., pp. 215-225, 1986.
  31. Stern, P.H. and Hoffman, R.M. Enhanced in vitro selective toxicity of chemotherapeutic agents for human cancer cells based on a metabolic defect. *J. Natl. Cancer Inst.* **76**, 629-639, 1986.
  32. Freeman, A.E. and Hoffman, R.M. In vivo-like growth of human tumors in vitro. *Proc. Natl. Acad. Sci., USA* **83**, 2694-2698, 1986.
  33. Stern, P.H. and Hoffman, R.M. The chemical synthesis of high specific-activity [<sup>35</sup>S]adenosylhomocysteine. *Analytical Biochem.* **158**, 408-412, 1986.
  34. Vescio, R.A., Redfern, C.H., Nelson, T.J., Ugoretz, S. Stern, P.H. and Hoffman, R.M. *In vivo*-like drug responses of human tumors growing in three-dimensional, gel-supported, primary culture. *Proc. Natl. Acad. Sci., USA* **84**, 5029-5033, 1987.
  35. Hoffman, R.M. Altered methionine metabolism and unbalanced methylation: a possible basis for the dynamic phenotype of cancer. *Absorption and Utilization of Amino Acids*, (1989) CRC Press, Boca Raton, Florida M. Friedman (ed.) pp. I -7.
  36. Hoffman, R.M., Monosov, A.Z, Connors, K.M., Herrera, X. and Price, J.H. A general native-state method for determination of proliferation capacity of human normal and tumor tissues *in vitro*. *Proc. Natl. Acad. Sci., USA* **86**, 2013-2017, 1989.
  37. Wallen, J.W., Cate, R.L., Kiefer, D.M., Riemen, M.W., Martinez, D., Hoffman, R.M., Donahoe, P.K., Von Hoff, D.D., Pepinsky, B. and Oliff, A. Minimal antiproliferative effect of recombinant Mullerian Inhibiting Substance on gynecological tumor cell lines and tumor explants. *Cancer Res.* **49**, 2005-2011, 1989.
  38. J.Vescio, R.A., Connors, K.M., Youngkin, T., Bordin, G.M, Robb, J.A, Umbreit, J.N. and Hoffman, R.M. Cancer biology for individualized cancer therapy: Correlation of growth

- fraction index in native-state histoculture with tumor grade and stage. Proc. Natl. Acad. Sci., USA **87**, 691-695, 1990.
39. Hoffman, R.M. Unbalanced transmethylation and the perturbation of the differentiated state leading to cancer. BioEssays **12**, 163-166, 1990.
  40. Vescio, R.A., Connors, K.M., Bordin, G.M., Robb, J.A., Youngkin, T, Umbreit, J.N. and Hoffman, R.M. The distinction of small cell and non-small cell cancer by growth in native-state histoculture. Cancer Res. **50**, 6095-6099, 1990.
  41. Wilson, W.W. and Hoffman, R.M. Methylation of intact chromosomes by bacterial methylases in agarose plugs suitable for pulsed-field electrophoresis. Analytical Biochem. **191**, 370-375, 1990.
  42. Hoffman, R.M. *In vitro* sensitivity assays in cancer: A review, analysis and prognosis. J. Clin. Lab. Anal. **5**, 133-143, 1991.
  43. Li, L., Margolis, L.B. and Hoffman, R.M. Skin toxicity determined *in vitro* by three-dimensional, native-state histoculture. Proc. Natl. Acad. Sci. **88**, 1908-1912, 1991.
  44. Robbins, K.T., Varki, N.M., Storniolo, A.M., Hoffman, H. and Hoffman, R.M. Drug response of head and neck tumors in native-state histoculture. Archives of Otolaryngol. Head and Neck Surg. **117**, 83-86, 1991.
  45. Hoffman, R.M. Three-dimensional histoculture: Origins and applications in cancer research. Cancer Cells **3**, 86-92, 1991.
  46. Vescio, R.A., Connors, K.M., Kubota, T. and Hoffman, R.M. Correlation of histology and drug response of human tumors grown in native-state three-dimensional histoculture and in nude mice. Proc. Natl. Acad. Sci., USA **88**, 5163-5166, 1991.
  47. Guadagni, F., Roselli, M. and Hoffman, R.M. Maintenance of expression of tumor antigens in three-dimensional *in vitro* human tumor gel-supported histoculture. Anticancer Res. **11**, 543-546, 1991.
  48. Hoffman, R.M. Three-dimensional gel-supported native-state histoculture for evaluation of tumor-specific pharmacological activity: Principles, practices and possibilities. J. Cell. Pharmacol. **2**, 189-201, 1991.
  49. Li, L. and Hoffman, R.M. Hair growth and hair follicle-cell proliferation in histocultured mouse skin. Annals of the New York Academy of Sciences, The Molecular and Structural Biology of Hair. **642**, 506-509, 1991.
  50. Fu, X., Besterman, J.M., Monosov, A. and Hoffman, R.M. Models of human metastatic colon cancer in nude mice orthotopically constructed by using histologically-intact patient specimens. Proc. Natl. Acad. Sci., USA **88**, 9345-9349, 1991.



51. Li, L., Margolis, L.B. and Hoffman, R.M. Native-state sponge-gel histoculture of intact 3-dimensional tissue for *in vitro* toxicity assays. *Alternative Methods in Toxicology*, 8th International CAAT Symposium, (ed.) Alan M. Goldberg, The Johns Hopkins University. Vol. 8, 311-316, 1991.
52. Fu, X., Theodorescu, D., Kerbel, R.S. and Hoffman, R.M. Extensive multi-organ metastasis following orthotopic onplantation of histologically-intact human bladder carcinoma tissue in nude mice. *Int J. Cancer* **49**, 938-939, 1991.
53. Baibakov, B., Frank, G.A., Sergeeva, N., Youngkin, T., Connors, K.M., Hoffman, R.M. and Margolis, L.B. *In vivo* growth patterns of human lung tumors in three-dimensional histoculture. *In Vitro Cell Dev. Biol.* **27A**, 897-899, 1991.
54. Hoffman, R.M. Altered regulation of transmethylation and loss of organotypic behavior in cancer. *Korean J. Biochem.* **23**, 83-89, 1991.
55. Li, L. and Hoffman, R.M. Eye tissues grown in three-dimensional histoculture for toxicological studies. *J. Cell. Pharmacol.* **2**, 311-316, 1991.
56. Furukawa, T., Kubota, T., Watanabe, M., Takahara, T., Yamaguchi, H., Takeuchi, T., Kase, S., Kodaira, S., Ishibiki, K., Kitajima, M. and Hoffman, R.M. High *in vitro-in vivo* correlation of drug response using sponge-gel-supported three-dimensional histoculture and the MTT end point. *Int. J. Cancer* **51**, 489-498, 1992.
57. Fu, X., Guadagni, F. and Hoffman, R.M. A metastatic nude-mouse model of human pancreatic cancer constructed orthotopically from histologically-intact patient specimens. *Proc. Natl. Acad. Sci., USA* **89**, 5645-5649, 1992.
58. Guadagni, F., Li, L. and Hoffman, R.M. Targeting antibodies to live tumor tissue in 3-D histoculture. *In Vitro Cell. & Dev. Biol.* **28A**, 297-299, 1992.
59. Fu, X. and Hoffman, R.M. Human RT-4 bladder carcinoma is highly metastatic in nude mice and comparable to ras<sup>H</sup>-transformed RT-4 when orthotopically onplanted as histologically-intact tissue. *Int. J. Cancer* **51**, 989-991, 1992.
60. Wang, X., Fu, X. and Hoffman, R.M. A new patient-like metastatic model of human lung cancer constructed orthotopically with intact tissue via thoracotomy in immunodeficient mice. *Int. J. Cancer* **51**, 992-995, 1992.
61. Colangelo, D., Guo, H-Y, Silvestro, L. and Hoffman, R.M. Non-colorimetric measurement of cell activity in three-dimensional histoculture using the tetrazolium dye MTT: The pixel image analysis of formazan crystals (PIAFC). *Analytical Biochem.* **205**, 8-13, 1992.
62. Guo, H-Y., Colangelo, D., Li, L., Connors, K.M., Kubota, T. and Hoffman, R.M. *In vitro* histoculture of human tumors with fluorescent dye end-points measured by confocal microscopy: High correlation of *in vitro* and *in vivo* chemosensitivity. *Anticancer Res.* **12**, 1055-1062, 1992.

63. Hoffman, R.M. Patient-like models of cancer in mice: A review and critique of their development. *Current Perspectives on Molec. & Cell. Oncol.* **1**, Part B, 311-329, 1992.
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